UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,830	01/30/2002	Yizhong Gu	PB0169	3442

7590 06/15/2005

Stephen G. Ryan
Amersham Biosciences
800 Centennial Avenue
Piscataway, NJ 08855

EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/060,830
Filing Date: January 30, 2002
Appellant(s): GU ET AL.

Yonggang Ji
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed April 13, 2005.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

Appellant's brief includes a statement that there are no related appeals or interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is not correct. Claims 1 and 3-47 are pending. Claims 2, 48, and 49 are canceled. Claims 13-31, 34-38, 40-47 are withdrawn. Claims 1, 3-12, 32, 33, and 39 are rejected

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct. However, the summary contains an abbreviation, LCP, which is not defined. For the benefit of the Board, the examiner notes that LCP is defined on page 4, line 20, of the specification; as "LCCL domain containing protein (LCP)".

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Database EMBL 'Online! 3 March 2000 - retrieved from EBI - Database accession no. AI302412 XP002265294.

Database EMBL 'Online! 23 October 2000 - retrieved from EBI - Database accession no. BF037277 XP002265295.

Database EMBL 'Online! 21 October 2000 - retrieved from EBI - Database accession no. AW07902 XP002265296.

Database EMBL 'Online! 1 November 1996 - retrieved from EBI - Database accession no. Q14089 XP002265297.

Qatabase EMBL 'Online! 1 December 2001 - retrieved from EBI - Database accession no. Q96PD2 / XP002265298.

Database EMBL 'Online! 14 January 2001 - retrieved from EBI - Database accession no. AF387547 XP002265299.

Birren et al. Homo sapiens chromosome 3, clone RP11-319J24. EMBL # AC013497 26-MAR-2000 Alignment with SEQ ID NO: 4 and 6.

Hillier et al. The WashU-Merck EST Project. 09-NOV-1995 EST#H80005 Alignment with SEQ ID NO: 1115.

Iwanaga et al. Molecular mechanism of hemolymph clotting system in Limulus. Thromb Res. 1992 Oct 1;68(1):1-32. Review.

Kobuke et al. ESDN, a novel neuropilin-like membrane protein cloned from vascular cells with the longest secretory signal sequence among eukaryotes, is up-regulated after vascular injury. J Biol Chem. 2001 Sep 7;276(36):34105-14. Epub 2001 Jul 10.

Koshikawa et al. Significant up-regulation of a novel gene, CLCP1, in a highly metastatic lung cancer subline as well as in lung cancers in vivo. Oncogene. 2002 Apr 25;21(18):2822-8.

Penn et al. Human Genome-derived single exon nucleic acid probes useful for gene expression analysis by miroarray. US Application 09/864,761. FD 23-MAY-2001. SEQ ID NO: 12400. Alignment with SEQ ID NO: 6.

Robertson et al. Mutations in a novel cochlear gene cause DFNA9, a human nonsyndromic deafness with vestibular dysfunction. Nat Genet. 1998 Nov;20(3):299-303.

Rosteck et al. Factor 8 homolog polypeptides and nucleic acids encoding them for treating coagulation related disorders such as hemophilia and stroke. WO 200012532 09-MAR-2000 N_geneseq Acc#AAZ51872. Alignment with SEQ ID NO: 4 and 6.

Old RW and Primrose SB. Nucleic acid hybridization methods. In: Principles of Gene Manipulation. Blackwell Scientific Pubs. Boston, MA pages 117-120.

Schena, M et al. Parallel human genome analysis: Microarray-based expression monitoring of 1000 genes. Proc Natl Acad Sci U S A. 1996 Oct 1;93(20):10614-9.

Trexler et al The LCCL module. Eur J Biochem. 2000 Sep;267(18):5751-7.

Wishart et al, A single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. J Biol Chem. 1995 Nov 10;270(45):26782-5.

Witkowski et al, Conversion of a beta-ketoacyl synthase to a malonyl decarboxylase by replacement of the active-site cysteine with glutamine. Biochemistry. 1999 Sep 7;38(36):11643-50.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

Claims 1, 3-12, 32, 33, and 39 are rejected under 35 U.S.C. §101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1, 3-12, 32, 33, and 39 are directed to isolated polynucleotides encoding proteins which share sequence similarity to the CUB, LCCP, and DSD/FA58C domains of other proteins. Based on structural similarity, the specification asserts that the claimed polynucleotides encode LCCL domain containing proteins (LCPs). The specification fails to assert a specific biochemical activity or function for LCP or for polynucleotides encoding LCP. The specification does assert that LCP plays a role in the autosomal recessive deafness disease DFNH9 and/or myotonic dystrophy 2. The specification states that the instant polypeptide is

important for neurological and developmental disorders as well as diseases involving cell-cell adhesion and are a cause of human diseases involving the adrenal, liver, bone marrow, brain, liver, heart, kidney, lung, placenta, skeletal muscle, colon, or prostate. The specification goes on to state that the polynucleotides and antibodies to polypeptides of the instant invention can be used as probes to assess the levels in adrenal, liver, bone marrow, brain, liver, heart, kidney, lung, placenta, skeletal muscle, colon, or prostate in order to diagnose neurological and developmental disorders as well as diseases involving cell-cell adhesion. The specification also proposes that the recited nucleic acids have utility as hybridization probes, for anti-sense inhibition of expression, in microarrays, to prime synthesis of nucleic acids, for cDNA-mRNA subtraction, for in vitro translation, to express the encoded protein, to target homologous recombination, and as commercial products.

The claimed invention does not meet the utility requirements for the following reasons.

The specification fails to disclose either a specific and substantial asserted utility or a well-established utility for the recited nucleic acid molecules and encoded proteins. The evidence recited in the specification for LCP being involved in DFNH9 deafness disease is that (i) the LCP gene maps to a region of the human chromosome, 3q12.1, within the 3q region for the DFNH9 gene and (ii) that mutation in the LCCL-domain of a known cochlear protein, COCH, causes DFNH9. The prior art teaches that mutations of COCH are responsible for DFNH9 deafness because COCH maps to the locus for DFNH9 and individuals with DFNH9 have mutations within the LCCL domain of COCH (Roberston et al, 1998). However, the fact that LCP has a LCCL domain, maps near the locus for DFNH9, and that mutation within the LCCL domain of COCH causes DFNH9 is not sufficient evidence for a person of ordinary skill

in the art to conclude a credible role for LCP in DFNH9 deafness. COCH and LCP are distinct genes; the linkage of COCH to DFNH9 deafness does not mean that any gene encoding a common peptide domain, such as the LCCL domain, is also linked to DFNH9 deafness. Appellant's assertion that LCP plays a role in myotonic dystrophy 2 is based simply on the fact that this disease also maps to the 3q region of the human chromosome. Again, the correlation between the location for LCP gene and myotonic dystrophy 2 is not sufficient to be convinced of a credible role for LCP in this disease, especially in light of the fact that other diseases, for example DFNH9, maps to the same region. The proposed utilities for the LCP gene and encoded proteins in these diseases are not supported by any demonstrated role for the recited polynucleotides and proteins encoded thereby in either DFNH9 deafness or myotonic dystrophy 2. Furthermore, these asserted utilities are not supported by a deduced function for said polynucleotides and proteins, as evidenced by the function of known LCP proteins, for example, in non-human species. Thus, these asserted utilities for the recited polynucleotides are neither specific as, a large number of human DNAs are associated with any region of the chromosome, nor credible as no demonstrated or deduced function has been has been shown. Without such evidence, a utility for LCP in the diagnosis and/or treatment of DFNH9 deafness and/or myotonic dystrophy 2 is not credible.

Clearly, at the time of filing, further experimentation was needed to provide sufficient evidence as to the utility of the recited invention. In fact, subsequent to filing of the instant Application, further experimentation by Koshikawa et al, 2002 disclosed that the protein recited in the instant invention can be used as a marker for metastatic lung cancer. However, said specific utility was not asserted in the instant Application. The long laundry list of diseases and

disorders the recited polypeptide might be involved in, as stated above, is not an assertion of what the function of recited polynucleotide is.

Regarding the recited nucleic acids having utility as hybridization probes, for anti-sense inhibition of expression, in microarrays, to prime synthesis of nucleic acids, for cDNA-mRNA substraction, for in vitro translation, to express the encoded protein, to target homologous recombination, and as commercial products, as stated above, each of these utilities is an application which would apply to every member of a general class of materials and/or is a use only for further research to determine a use for the recited nucleic acid molecules or the proteins encoded thereby. As such, these asserted utilities are not specific (for those applicable to all human DNAs) or not substantial because the use of the recited polynucleotides therein is only potential and not in currently available in practical form. Without knowledge of a function for the recited polynucleotide and the encoded proteins, one of skill in the art would not be motivated use them in the recited assays.

Thus, Claims 1, 3-12, 32, 33, and 39 are rejected under 35 U.S.C. §101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claim Rejections - 35 USC §112, first paragraph

Claims 1, 3-12, 32, 33, and 39 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Arguments

A. Do Claims 1, 3-12, 32, 33, and 39 lack a patentable utility?

In support of their request that rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. §101 be withdrawn, Appellants provide the following arguments.

(A.) For newly discovered compounds that belong to a class of compounds, the members of which have become well recognized as useful for a particular purpose because of a particular property, the only reasonable conclusion is that the new compound also possessing that property is similarly useful, as per Folkers at 975 and MPEP 2107.02. The recited nucleic acid sequence encodes a trans-membrane human LCP protein comprising an N-terminal signal peptide, an LCCL domain, a discoidin domain, a predicted amphipathic, membrane binding alpha helical structure at the C-terminal, and a truncated CUB domain. Mutations within the LCCL domain of COCH have been shown to cause the deafness disorder DFN9 in humans, while the CUB domain is found mostly in developmentally regulated proteins. Appellants submit that the gene and encoded polypeptides of the instant invention are useful in developing therapeutics as well as diagnostics for neurological and developmental disorders and tumors.

(B.) The teachings of Koshikawa et al support Appellants' assertion that the recited gene and encoded polypeptides have utility in developing therapeutics as well as diagnostics for neurological and developmental disorders and tumors.

(C.) It is well-established that any gene can be used for disease diagnosis, prognosis, and in the development of therapeutics. Furthermore, the polynucleotide of any gene can be used as reference to compare to gene sequences from patients or healthy individuals for mutational analysis. LCP is clearly capable of the same use. The nucleic acid sequences can be used as substrates on microarrays, for expression analysis, including in cancer patients or

patients with developmental disorders. Human whole genome microarrays containing every human gene are now commercially available. The usefulness of said arrays have been demonstrated by thousands of groups.

(D.) The claimed nucleic acids can also be used as antisense inhibitors of the over-expressed genes in patients, to produce proteins, antibodies or fusion proteins useful for the diagnosis and development of therapeutics. The nucleic acids can also be used to develop primers and probes, which can be used in PCR amplification of fragments of the gene, while the probes can be used for genomic as well as expression analysis

(E.) According to the Federal Circuit, the threshold of utility is not high: an invention is useful under section 101 if it is capable of providing some identifiable benefit. Thus, Appellants submit that Examiner's rejections cannot be sustained.

These arguments are not found to be persuasive for the following reasons.

(A) Reply It is acknowledged that if a polynucleotide encodes polypeptide that has a high level of similarity with a protein known to have a specific function, a person of ordinary skill in the art would conclude said polypeptide has the same specific function. However, at the time of filing, the polypeptide of the instant application was not known to be highly homologous to any protein with a well-established, specific function. The presence of certain domains in the instant polypeptide gives some insight into what the function of said polypeptide might be, but does not establish what the function is. Furthermore, just because mutation in the LCCL domain of COCH causes a deafness disorder would not convince one of skill in the art that mutation of the LCCL domain of the protein encoded by the recited polynucleotide causes a deafness disorder. COCH and LCP are distinct genes. Linkage of COCH to DFNH9 deafness does not

mean that, because LCP, like COCH, has a LCCL domain, LCP is also linked to DFNH9 deafness.

(B) Reply It is acknowledged that Koshikawa et al teach that the instant protein can be used as a marker for metastatic lung cancer. However, said specific utility was not asserted in the instant application. The specification states that the instant polypeptide is important for neurological and developmental disorders as well as diseases involving cell-cell adhesion and are a cause of human diseases involving the adrenal, liver, bone marrow, brain, liver, heart, kidney, lung, placenta, skeletal muscle, colon, or prostate. The specification goes on to state that the polynucleotides and antibodies to polypeptides of the instant invention can be used as probes to assess the levels in adrenal, liver, bone marrow, brain, liver, heart, kidney, lung, placenta, skeletal muscle, colon, or prostate in order to diagnose neurological and developmental disorders as well as diseases involving cell-cell adhesion. Such a laundry list of diseases and disorders the recited polypeptide might be involved in is not an assertion of what the function of said polypeptide is and, furthermore, is not an assertion that the recited polynucleotide and encode polypeptides are markers for metastatic lung cancer.

(C) Reply It is acknowledged that the use of polynucleotides in DNA chips (microarrays) is widespread and that the claimed polynucleotides can be attached to DNA chips. However, for the claimed polynucleotides to be specifically useful in such application, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking the expression patterns of such polynucleotides. The reduction or increase in expression of a polynucleotide is meaningless unless one can link changes in expression with some biological function. For

example, if one were to use the claimed polynucleotides in assays which would lead to the discovery of drugs of a specific condition, such as an assay which uses a DNA chip to evaluate expression patterns upon exposure to a test compound, one would need to know which diseases and/or biological functions are associated with the expression of such polynucleotides. Otherwise, one of skill in the art would have to carry out further experimentation to determine which are the specific conditions (i.e. diseases) and/or biological functions associated with the claimed polynucleotides. Appellant's asserted utility of the claimed polynucleotides as specific markers which are targets for discovering therapeutics and treatments associated with human disease is not a specific and substantial utility since the specification is silent in regard to (1) the specific conditions and/or biological functions which are associated with the expression of the claimed polynucleotides, (2) whether increase or decrease in expression correlates with disease, and (3) which levels of increase or decrease in expression of the claimed polynucleotides are indicative of the presence or absence of a disease. This is analogous to the examples provided by MPEP § 2107.01 in regard to what constitutes carrying out further research to identify or reasonably confirm a "real world" context of use, since basic research is required to determine the properties or the mechanisms in which the claimed product is involved. The asserted use of the claimed polynucleotides in DNA chips is not specific since, as Appellants have stated, many other polynucleotides including those in the public domain can and are used in DNA chips.

(D) Reply It is acknowledged that the claimed polynucleotides can be used as antisense inhibitors, to produce proteins, antibodies or fusion proteins, and to develop primers and probes. However, said uses do not have patentable utility. As is well known to anyone skilled in the art, any polynucleotide can be used in such applications and, thus, said uses are not

specific to the recited nucleic acid molecules. Without knowing the diseases or disorders caused by over expression of the polypeptide encoded by the recited nucleic acid molecules one would not know which patients to treat with anti-sense inhibitors derived from the recited sequences. Likewise, one would not know which disease or conditions to diagnose with the recited polynucleotides or antibodies to the encoded proteins. A person of ordinary skill in the art would not be motivated to use the recited polynucleotides in PCR amplification without knowing the function of the gene or encoded protein. The specification fails to describe the use of the recited nucleic acid molecule as a gene marker for any disease. Regarding the use for analysis of expression, see above discussion on microarrays (C). Thus, these asserted uses are not specific, because they are applicable to all human DNAs, or not substantial because the use of said polynucleotides and proteins therein is only potential and not in currently available in practical form, because the functions of the gene and encoded protein are unknown.

(E) Reply The instant specification fails to provide sufficient evidence to support any patentable utility for the recited polynucleotides and encoded polypeptides. The instant application merely discloses the structure of the claimed polynucleotides and no biological characterization of the polypeptide encoded by the claimed polynucleotide other than to state that, based on sequence homology, it appears to be an LCP, i.e. an LCCL domain containing protein. Even if one assumes that the polypeptide encoded by the claimed polynucleotides is an LCP, the specification fails to provide sufficient information for one of skill in the art to know how to use the claimed invention. The specification is silent in regard to (1) the biochemical activity of the polypeptide being encoded by the claimed polynucleotides, (2) the biological processes or pathways in which the recited protein is involved, (3) the specific molecular

interactions associated with the recited protein, or (4) any diseases linked to mutation of the recited polynucleotides and encoded proteins, such that a specific use for the claimed polynucleotides would be apparent. A skilled artisan cannot reasonably conclude that the claimed polynucleotides have a specific and substantial, or even credible utility in view of the evidence presented.

B. Are Claims 1 and 3 unusable due to a lack of patentable utility?

Appellants submit that, because the claim invention has patentable utility, a person of ordinary skill in the art would know how use the recited polynucleotides and encoded polypeptides.

Reply As indicated by Appellants, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

Therefore, for reasons set forth above, Appellants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and it is believed that the rejections should be sustained.

Respectfully submitted,

Sheridan Swope, Ph.D.
Art Unit 1652

June 2, 2005

Conferees

Ponnathapura Achutamurthy, Ph.D.
SPE, Art Unit 1652

Bruce Campell
SPE, Art Unit 1654

YONGGANG JI
AMERSHAM BIOSCIENCES CORPORATION
800 CENTENNIAL AVENUE
P. O. BOX 1327
PISCATAWAY, NEW JERSEY 08855-1327

Sheridan Swope, Ph.D.
Patent Examiner
Recombinant Enzymes-Art Unit 1652
USPTO
Remsen Bld
400 Dulaney St.
Alexandria, VA 22314-5774
571-272-0943
sheridan.swope@uspto.gov